REMARKS

The present application is directed to a method of detecting the presence of a target nucleic acid in a sample. Claims 43, 46, 48-69 and 87-88 are pending.

Rejection of Claims under 35 U.S.C. § 102(b)

The Examiner rejects Claims 43, 48-53 and 57-69 under 35 U.S.C. § 102(b) as anticipated by European Patent Publication EP 0 872562 A1 ("Higuchi"). Applicants respectfully traverse the rejection. MPEP 2131 provides: "To anticipate a claim, the reference must teach each and every element of the claim." Applicants respectfully assert that Higuchi fails to anticipate the rejected claims because it fails to teach at least one element of these claims.

The Examiner's interpretation of Higuchi is set forth in the paragraph bridging pages2-3 of the Office Action. Applicants assert that the element identified as (a) by the Examiner contains at least one error. Specifically, the Examiner asserts that Higuchi teaches "a DNA binding agent which can absorb fluorescent energy from the fluorescent label on the probe." Applicants respectfully disagree.

The basis of the method taught in Higuchi is that a DNA binding agent such as daunomycin can be used, independently, as a measure of amplification. Suitable DNA binding agents include intercalating dyes, which combine with double stranded DNA, but produce a distinguishable signal when bound, as compared to when they are unbound. Therefore, as the total amount of double stranded DNA present in the reaction increases as a result of amplification, the signal from the DNA binding agent will change, thus giving an indication of the progress of the amplification. *See*, for example, Higuchi, page 4, line 44, through page 5, line 3; page 8, lines 29-37.

The section of Higuchi found on page 5 lines 24-33, which the Examiner cites on page 3 of the Office Action, suggests that the basic method, as discussed above, may be used "in conjunction" with a system of oligonucleotide probes. The system of oligonucleotide probes taught in Higuchi is a dual-labeled probe system, which internally **contains both a quencher**

and a fluorophore, such as is used in the "TaqMan(TM)" probe system. This is clear from the passage on page 5, lines 27-30, of Higuchi, which states (emphasis added):

> The probe, **labeled with a quencher and fluorophore**, hybridizes to the amplified target nucleic acid. In the presence of an agent for polymerization capable of 5' to 3' nucleolytic activity, the fluorophore and quencher, when bound to the target, are **separated by degradation** of the probe by the polymerase. The fluorescence of the unbound probe is detectably distinct from the fluorescence of the bound, and subsequently hydrolyzed probe.

Is it clear from this description provided in Higuchi that the probe signal is dependent solely on probe hydrolysis and the separation of the two moieties that the probe carries, the fluorophore and the quencher. The quencher, which is present on the probe itself, but not the DNA binding agent, is required to absorb fluorescent energy from the fluorophore of the probe. Applicants assert that, if, in the method disclosed in Higuchi, the DNA binding agent were to do absorb fluorescent energy from the probe, it would interfere with the signal from the probe.

Effectively, Higuchi teaches that there are two independent signaling systems present, one based upon a DNA binding agent and one based upon a dual-labeled probe. This is evidenced by the statement on page 5, line 30, of Higuchi:

> "Thus, the fluorescence of the DNA binding agent enables detection that amplification has occurred, and the fluorescence of the hybridized probe indicates target specific amplification."

Therefore, the two independent signaling systems, as disclosed in Higuchi, provide distinct information. Applicants assert that, if the two systems were to interact with each other in the manner proposed by the Examiner, they would effectively interfere with each other's signals, making the results less reliable.

Applicants respectfully assert that Higuchi fails to anticipate the pending claims at least because it fails to teach at least one element of the claims, namely, a DNA binding agent which can absorb fluorescent energy from the fluorescent label on the probe. Applicants therefore request withdrawal of the rejection.

Rejection of Claims for Reasons of Nonstatutory Obviousness-Type Double Patenting

The Examiner rejects Claims 43, 46, 48-69 and 87-88 on the ground of nonstatutory obviousness-type double patenting as unpatentable over Claims 1-13 of U.S. Patent 6,833,257 (commonly owned with the present application) in view of Higuchi. Applicants respectfully traverse the rejection.

In summary, the Examiner asserts on pages 4-5 of the Office Action that the only difference between the disclosure provided in U.S. Patent 6,833,257 and the present case is that the DNA binding agents used in the claims are mitoxantrone and daunomycin, and that daunomycin at least is taught in Higuchi as a possible DNA binding agent.

However, as discussed in the previous section of this Response, in the method taught Higuchi, the DNA binding agents are used for detecting amplification by detecting bulk increases in double stranded DNA in non-specific way. According to the disclosure of Higuchi, the DNA binding agents are not required to interact with other fluorophores, including those present on the probes. Applicants therefore assert that not have been obvious to one of ordinary skilled in the art in the area of the present application, at its priority date, to select DNA binding agents proposed in Higuchi for use in the assay disclosed in U.S. Patent 6,833,257, where they DNA binding agents are specifically **required to interact with a fluorophore on a probe**.

Applicants discovered and disclosed in the present application that the DNA binding agents recited in the pending claims, mitoxantrone and daunomycin, in fact, act extremely well as quenchers of probe fluorophores since their emissions are largely undetectable in the context of the method, and, therefore, there is less need for signal resolution. Applicants accordingly assert that, at least due to the above unexpected advantage of the claimed embodiments of applicants' method, the rejected claims are unobvious in view of the combination of the cited claims of U.S. Patent 6,833,257 and the disclosure of Higuchi. Applicants respectfully request withdrawal of the rejection.

CONCLUSION

This response fully addresses the rejections in the Office Action of September 2, 2009. In light of the above remarks, applicants respectfully assert that the application is now in condition for allowance. Such action is respectfully requested.

If the Examiner believes any informalities remain in the application that may be corrected by Examiner's Amendment, or if there are any other issues that can be resolved by telephone interview, a telephone call to the undersigned agent at (404) 815-6102 is respectfully solicited. No additional fees are believed due; however the Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account number 11-0855.

Respectfully submitted,

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